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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/331,980	11/26/99	CHAGNAUD J	19141-006

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IVOR R ELRIFI
MINTZ LEVIN COHN FERRIS
GLOVSKY & POPEO
ONE FINANCIAL CENTER
BOSTON MA 02111

EXAMINER	
HUYNH, P	
ART UNIT	**PAPER NUMBER**
1644	10

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/331,980	CHAGNAUD ET AL.	
	Examiner	Art Unit	
	" Neon" Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11/26/99; 9/18/00; 5/7/01* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 7-14* is/are pending in the application.

4a) Of the above claim(s) *7-10,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,11 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Claims 12-23 are pending.

2. Applicant's election with traverse of Group I claims 1-5, 11 and 14, filed 5/7/01, is acknowledged. The traversal is on the ground that the claimed isolated antibody recognizing a nitrosylated protein (NO) while the reference Ye et al teach antibodies directed against nitrated proteins (NO2). However, Bollerne *et al* teach purified polyclonal antibodies to Nitrosylated protein (See NO-Cys-g-BSA in **Materials and Methods**, pp. 118-119, in particular). The requirement is still deemed proper and is therefore made FINAL.

3. Claims 7-10, 12-13 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-5, 11 and 14 are being acted upon in this Office Action.

5. Applicant should amend the first line of the specification to update the status of the priority documents. For example, This Application is a 35 U.S.C 371 national application of PCT/FR97/02412, filed 12/23/97.

6. It is noted that the specification mentioned figures 1-15 throughout the specification. However, none of the drawings have been supplied to the Office.

7. The specification is objected to because of the following informality. Correction is required in the specification, See "." at the beginning of a sentence throughout the specification. Also, the phrase "N0-Tyr-BSA" on page 54, line 5 should have been "NO-Tyr-BSA" and the word "et" on page 43 line 10 should be "and". Appropriated correction is required.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

9. Claims 2, 4-5, 11 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The phrase "characterized by the fact" as recited in claims 2, 4-5, 11 and 14 are unclear. The term is unclear what characteristics are to be included or excluded. One of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention. It is suggested that applicant amends the claim to include functional limitations using the Markush language, See MPEP §§ 2173.05(h).

The phrase "A pharmaceutical compound" as recited in claim 11 is ambiguous and one of ordinary skill in the art cannot appraise the metes and bounds of the claimed invention. As written, the pharmaceutical compound is the antibody **conjugated** to an acceptable carrier and not a composition. It is suggested that applicant amend the claim to recite "a composition consisting of antibody that binds specifically to nitrosylated...and a pharmaceutical carrier or excipients".

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4 are rejected under 35 U.S.C. 102(b) as being anticipated by Boullerne *et al.* (J. of Neuroimmunology 60: 117-124, 1995; PTO 892).

Boullerne *et al* teach a purified antibody that recognizes a nitrosylated protein (nitrosylated bovine serum albumin). The immunogen is composed of a nitrosylated carrier protein (nitrosylated bovine serum albumin) or a nitrosylated amino acid (cysteine) coupled to a carrier (bovine serum albumin) by a coupling agent which is glutaraldehyde (g) (See NO-Cys-g-BSA in **Materials and Methods**, pp. 118-119, in particular). Antibody to the nitrosylated bovine serum albumin can be use in Enzyme-linked immunosorbent Assay (ELISA) to detect nitrosylated protein in the sera of patients with multiple sclerosis (See page 119, column 1, in particular). Boullerne *et al* further teach that NO production may be involved in autoimmune diseases including IDDM, SLE, autoimmune neuropathy of Chagas' disease caused by trypanosoma cruzi and the use of conjugated haptens (nitrosylated cysteine cross-linked to BSA) is very helpful in defining the specific antibody responses (See page 123, column 1, last paragraph, in particular). Applicants are notified that "characterized by the fact that" as recited in

claims 1, 4, 5, 11 and 14 does not further limit claim 1. Thus, the reference teachings anticipate the claimed invention.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-3, 5 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler *et al.*, (Proc. Natl. Acad. Sci USA 89: 444-448, 1992; PTO 892) or U.S. Pat No. 5,583,101 (PTO 892) each in view of Campbell *et al* (Monoclonal antibody technology , Elsevier Science Publishers, 1984).

Stamler *et al* teach a method of synthesizing S-Nitroso proteins wherein the proteins include BSA, t-PA, Cathepsin B and human plasma. Stamler *et al* further teach nitric oxide (NO) has a half-life in the order of 0.1 second *in vivo* and nitrosylation of NO increases the half-life of these NO molecules to about 24 hour (See page 444, column 1, 1st paragraph; page 445, column 2 Results; page 446, column 1, last paragraph, in particular).

'101 teaches a pharmaceutical compound as recited in claim 11 (See column 1, line 39; column 6, line 51, in particular). Applicants are notified that "characterized by the fact that" as recited in claim 11 does not further limit claim.

The references do not teach antibodies to nitrosylated protein.

Campbell et al teach that "[i] it is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)" (See page 29, section "Basic research", in particular).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to make antibodies specific for nitrosylated protein comprising a transporter of NO coupled to a carrier protein such as albumin via a coupling agent such as glutaraldehyde. One would have been motivated, with a reasonable expectation of success, to generate monoclonal antibodies to nitrosylated protein based on the fact that it is a conventional practice in the art to so for further study, characterization, detection and diagnostic assays.

15. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stamler *et al.*, (Proc. Natl. Acad. Sci USA 89: 444-448, 1992; PTO 892) or U.S. Pat No. 5,583,101 (PTO 892) each in view of Campbell *et al* (Monoclonal antibody technology , Elsevier Science Publishers, 1984) as applied to claims 1-3, 5 and 11 above, and further in view of U.S. Pat No. 5,858,682 (Jan 1999, PTO 892; see entire document).

The combined teachings of the references have been discussed supra.

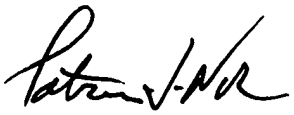
The claimed invention in claim 14 differs from the references only by the recitation of a kit comprising antibody for detection of any nitrosylated proteins in a biological specimen.

'682 teaches a kit comprising antibody for diagnostic (See column 3, line 40; column 6, line 17; column 8, line 36, in particular). '682 further teaches

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the antibody in a kit taught by '682 with the antibody that binds nitrosylated protein taught by Stamler, '101 and Campbell for the purpose of detecting nitrosylated protein immune complex in any biological specimen. One would have been motivated, with a reasonable expectation of success, to place the antibody in a kit for convenience and commercial expedience. A kit will allow for ease of use for the practitioner since all the necessary reagents, standard and instructions for use are included in a kit as taught by '682 (See column 8, line 36-57, in particular).

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.



Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
June 14, 2001

Patrick J. Nolan, Ph.D.
Primary Examiner
Technology Center 1600